

Information Resources for Clinical Research: A Brief Overview

July-Aug 2017, NIH Library, Bldg. 10 / Clinical Center

Josh Duberman, MLIS

Informationist / Research Librarian

jduberman@nih.gov

Healthy volunteer died after hexamethonium administration by inhalation

PI didn't find potential toxicity despite

- “standard PubMed search” &
- consulting “standard current editions of textbooks of pharmacology & pulmonary medicine”

- JHU Report, 7/01: *Report of Internal Investigation into the Death of a Volunteer Research Subject*, Johns Hopkins University, 7/01, https://web.archive.org/web/20150311234613/http://www.hopkinsmedicine.org/press/2001/JULY/report_of_internal_investigation.htm
- J Savulescu and M Spriggs, The Hexamethonium Asthma Study and the Death of a Normal Volunteer in Research, *J. Med. Ethics*, 2002; 28;3-4, PMID 11834748, <http://jme.bmj.com/content/28/1/3.full>

JHU research oversight was improved

“requiring investigators to collaborate with a librarian and a pharmacist to strengthen literature searches... to help search appropriate databases for potential side effects.”

Hopkins Response to FDA Observations, JHMI Office of Communications and Public Affairs, 9/7/01,

<https://web.archive.org/web/20070903162020/http://www.hopkinsmedicine.org/press/2001/SEPTEMBER/010907A.htm>

Guidelines were established at JHU & elsewhere

Guidelines for Determining an Adequate and Comprehensive Literature Search of Drug and Device Safety for Use by Investigator and Institutional Review Boards, Institutional Review Board, Mount Sinai School of Medicine, 1/03,

http://www.mssm.edu/static_files/Old%20Sites/www.mssm.edu/cmca/pdf/SearchGuidelines.pdf

Overview of clinical information resources, scope and capabilities, with links to more information:

- introduction to information resources – characteristics & questions to ask
- PubMed, Embase & other databases, both free & subscription-based
- internet search engines & other information resources
- search tips & issues to consider when conducting or requesting an information search

Searching for **adverse effects** & **protocol development**; applicable to many other topics in clinical research

“Introduction to the Principles and Practice of Clinical Research”, NIH
Clinical Center course, <http://www.cc.nih.gov/training/training/ipPCR1.html>

lecture, 3/7/16 <http://videocast.nih.gov/launch.asp?19530>

- relevant chapters in textbook, “Principles and Practice of Clinical
Research” JI Gallin & FP Ognibene, eds., 3rd ed., Elsevier, 2012,
<http://www.sciencedirect.com/science/book/9780123821676>

- 3 - Researching a Bioethical Question
- 10 - Unanticipated Risk in Clinical Research – 1990s
fialuridine (FIAU) clinical trials at the NIH - also see “Review of
the Fialuridine (FIAU) Clinical Trials, FJ Manning & M Swartz,
eds., Institute of Medicine, National Academy Press, 1995
http://www.nap.edu/openbook.php?record_id=4887
- 32 - Writing a Protocol

- **Origin** — lab data or journal article or database or reference/textbook;
 - publication cycle of new research: idea (request funding):
 - > preliminary findings (letters to the editor, submit patent application to be published in 18 months)
 - > research report (conference literature)
 - > publish research (peer-reviewed journals)
 - > popularize research (newspapers, websites)
 - > repackaged research (reviews, texts, guidelines)
- **Content** — scope/ subjects covered / comprehensiveness; exactly what's in a record, full text or titles/abstracts/keywords
- **Capabilities** — search technology, interface & added features; wildcards, Boolean logic; thesaurus; cited references/similar items

- **Access** — readily available or must be ordered; “free” vs. fee
- **Business Model** — who pays? - affiliations/sponsorship/bias
- **Familiarity** — sources you know how to search / sources you’ve heard about
 - Are there other important sources, changes, or updates?

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- US National Library of Medicine (NLM) database** – refers to >27 M articles from >5,600 biomedical journals in 39 languages
- medicine, nursing, dentistry, veterinary medicine, allied health & pre-clinical sciences
 - currently includes references from 1940s - present, with some older items
 - free access online – www.pubmed.gov; **NIH staff should click ‘PubMed@NIH’ under ‘Quick Links / Databases’ at the NIH Library site <http://nihlibrary.nih.gov> to access full text of subscribed journals**
 - bibliographic database with author-provided abstracts
 - added indexing terms - MeSH (Medical Subject Headings) thesaurus
 - links to other resources

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- Search Aids available by clicking '*Help*' - online book

<http://www.ncbi.nlm.nih.gov/books/NBK3827/>

» *includes Quick Start & FAQs at lower left*



» '*PubMed Tutorials*' - web-based & interactive

- Online training, tutorials, webinars, instruction materials -

<https://learn.nlm.nih.gov/rest/training-packets/T0042010P.html>

- MeSH – added subject headings often change over time
- My NCBI – save searches, get updates while trial is in progress
- Filters - not always obvious; 'clinical trial' filters don't include all observational studies
- Advanced Search: Search Builder – combine search results;
Details - shows what was searched;
phrase (string) searching: " " is only sometimes accurate

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New articles from highly accessed journals

Ann Pharmacother (1)

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Cancer Res (3)

EMBO J (1)

J Biol Chem (13)

Trending Articles

PubMed records with recent increases in activity

CRISPR-Cas encoding of a digital movie into the genomes of a population of living bacteria. Nature. 2017.

The effects of moderate- versus high-load resistance training on muscle growth, body composition, and performance in collegiate women. J Strength Cond Res. 2017.

PubMed Commons

Featured comments

Modeling absence epilepsy in rats? @DepaulisAntoine et al critique analysis; author D Barth replies. bit.ly/2ulYNqk Jul 14

Bias in biobank analyses—@MarcusMunafo et al discuss potential impact of low response rates on association estimates bit.ly/2spEqrT

JHU internal investigation found different PubMed results depending on the terms searched

<u>Terms searched</u>		<u># Results</u>	<u># Useful</u>
hexamethonium inhalation lung injury	=>	0 hits	--
hexamethonium inhalation	=>	42 hits	0
hexamethonium lung	=>	not reported	3
hexamethonium lung toxicity	=>	4 hits	0
hexamethonium lung hypersensitivity	=>	16 hits	3
hexamethonium lung fibrosis	=>	3 hits	2

- possibly due in part to limited coverage of older material & MeSH term changes over time - see Hexamethonium entry <http://www.ncbi.nlm.nih.gov/mesh/68018738>

- JHU Report, 7/01

How Search Works – typically every word in record is indexed & the index is searched; success depends on:

- File content or scope
- ★ • Individual record content (bibliographic info, abstract if it's available, indexing/keywords)
- Problem of categories & group names - thesauri, classification schemes
- Transparency/reproducibility of search algorithms & processes
- Additional search terms automatically added – plurals, synonyms, etc.

Build concept-based searches - first broad, then narrow

- use synonyms & group similar concepts together, and
- take controlled vocabulary terms into account - for example:

(ganglionic blockers OR hexamethonium) AND lung

PubMed record - default format

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The hexamethonium asthma study and the death of a normal volunteer in research.

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Substances

[Ganglionic Blockers](#)

[Hexamethonium](#)

PubMed - Older Information

PubMed now covers back to mid-1940s with some earlier coverage; older information is available in print sources – 3 examples:

- “Lung Changes During Hexamethonium Therapy for Hypertension”, British Heart J., 1954 – key article but
 - ‘**toxicity**’ or ‘**adverse effects**’ not in PubMed record
- ‘hexamethonium lung’ occurs in titles of 2 articles from 1956 & 1962
 - **indexing included ‘toxicity’ or ‘adverse effects’**
- **Cited reference searching could provide additional access**
 - more recent articles refer to older articles
- *1966 and all that--when is a literature search done?*, F McLellan, *The Lancet*, August 25, 2001, v358 i9282 p646
<http://www.ncbi.nlm.nih.gov/pubmed/11530164>

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- ☐ [Anti-Hu antibodies activate enteric and sensory neurons.](#)
1. Li Q, Michel K, Annahazi A, Demir IE, Ceyhan GO, Zeller F, Komorowski L, Stöcker W, Beyak MJ, Grundy D, Farrugia G, De Giorgio R, Schemann M.
Sci Rep. 2016 Dec 1;6:38216. doi: 10.1038/srep38216.
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- ☐ [HIF-1α Plays a Critical Role in the Gestational Sidestream Smoke-Induced Bronchopulmonary Dysplasia in Mice.](#)
2. Singh SP, Chand HS, Gundavarapu S, Saeed AI, Langley RJ, Tesfaigzi Y, Mishra NC, Sopori ML.
PLoS One. 2015 Sep 11;10(9):e0137757. doi: 10.1371/journal.pone.0137757. eCollection 2015.
PMID: 26361040 [Free PMC Article](#)
[Similar articles](#)
- ☐ [Regulation of Cigarette Smoke Induction of IL-8 in Macrophages by AMP-activated Protein Kinase Signaling.](#)
3. Ko HK, Lee HF, Lin AH, Liu MH, Liu CI, Lee TS, Kou YR.
J Cell Physiol. 2015 Aug;230(8):1781-93. doi: 10.1002/jcp.24881.
PMID: 25503516
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- ☐ [\[The role of the adreno-cholinergic interaction in the pulmonary hemodynamics changes following myocardial ischemia\].](#)
4. Evlakhov VI, Poiasov IZ.
Ross Fiziol Zh Im I M Sechenova. 2014 Jun;100(6):750-8. Russian.

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[Effect of euphylline and hexamethonium on the [Sov Med. 1969]

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((("ganglionic blockers"
[Pharmacological Action] OR
"ganglionic blockers"[MeSH
Terms] OR ("ganglionic"[All
Fields] AND "blockers"[All

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Query Translation:

```
((("ganglionic blockers"[Pharmacological Action] OR "ganglionic blockers"[MeSH Terms] OR ("ganglionic"[All Fields] AND "blockers"[All Fields]) OR "ganglionic blockers"[All Fields]) OR ("hexamethonium"[MeSH Terms] OR "hexamethonium"[All Fields])) AND ("lung"[MeSH Terms] OR "lung"[All Fields]))
```

Result:

[303](#)

Translations:

ganglionic blockers	"ganglionic blockers"[Pharmacological Action] OR "ganglionic blockers"[MeSH Terms] OR ("ganglionic"[All Fields] AND "blockers"[All Fields]) OR "ganglionic blockers"[All Fields]
hexamethonium	"hexamethonium"[MeSH Terms] OR "hexamethonium"[All Fields]
lung	"lung"[MeSH Terms] OR "lung"[All Fields]

Database:

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User query:

(ganglionic blockers OR hexamethonium) AND lung

PubMed

hexamethonium AND (toxicity OR adverse effects OR poisoning)



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- ☐ [Sub-chronic lead exposure produces \$\beta_1\$ -adrenoceptor downregulation decreasing arterial pressure reactivity in rats.](#)

Toscano CM, Simões MR, Alonso MJ, Salas M, Vassallo DV, Fioretti M.

Life Sci. 2017 Jul 1;180:93-101. doi: 10.1016/j.lfs.2017.05.009. Epub 2017 May 9.

PMID: 28499935

[Similar articles](#)

- ☐ [Neutrophil Recruitment and Articular Hyperalgesia in Antigen-Induced Arthritis are Modulated by the Cholinergic Anti-Inflammatory Pathway.](#)

Kanashiro A, Talbot J, Peres RS, Pinto LG, Bassi GS, Cunha TM, Cunha FQ.

Basic Clin Pharmacol Toxicol. 2016 Nov;119(5):453-457. doi: 10.1111/bcpt.12611. Epub 2016 May 20.

PMID: 27098245

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- ☐ [The effect of nicotine on the expressions of the \$\alpha 7\$ nicotinic receptor gene and Bax and Bcl-2 proteins in the mammary gland epithelial-7 breast cancer cell line and its relationship to drug resistance.](#)

Aali N, Motalebi G.

Cell Mol Biol Lett. 2015 Dec;20(5):948-64. doi: 10.1515/cmbl-2015-0056.

PMID: 26812869

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- ☐ [Role of Efferent Sympathoadrenal Effects in Cooling-Induced Hemodynamic Perturbations in Rats: An Investigation by Spectrum Analysis.](#)

Liu YP, Lin YH, Lin CC, Lin YC, Chen YC, Lee PL, Tung CS.

Chin J Physiol. 2015 Oct 31;58(5):312-21. doi: 10.4077/CJP.2015.BAD317.

PMID: 26387655

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Use of C1300 neuroblastoma cells to evaluate the protective [J Pharm Sci. 1995]

Antagonization of tetramisole toxicity by hexamethonium. [Chimioterapia. 1987]

Prophylactic action of hexamethonium, trimethaphar [Fundam Appl Toxicol. 1986]

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("hexamethonium"[MeSH Terms]
OR "hexamethonium"[All
Fields]) AND (("toxicity"
[Subheading] OR "toxicity"[All
Fields]) OR ("adverse effects"

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hexamethonium AND (toxicity OR adverse effects OR poisoning) ×

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Query Translation:

```
("hexamethonium"[MeSH Terms] OR "hexamethonium"[All Fields])
AND ((("toxicity"[Subheading] OR "toxicity"[All Fields]) OR
("adverse effects"[Subheading] OR ("adverse"[All Fields] AND
"effects"[All Fields]) OR "adverse effects"[All Fields]) OR
("poisoning"[Subheading] OR "poisoning"[All Fields] OR
"poisoning"[MeSH Terms]))
```

Search

URL

Result:

365

Translations:

hexamethonium	"hexamethonium"[MeSH Terms] OR "hexamethonium"[All Fields]
toxicity	"toxicity"[Subheading] OR "toxicity"[All Fields]
adverse effects	"adverse effects"[Subheading] OR ("adverse"[All Fields] AND "effects"[All Fields]) OR "adverse effects"[All Fields]
poisoning	"poisoning"[Subheading] OR "poisoning"[All Fields] OR "poisoning"[MeSH Terms]

Database:

PubMed

User query:

hexamethonium AND (toxicity OR adverse effects OR poisoning)

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YouTube Tutorial

((hexamethonium AND (toxicity OR adverse effects OR poisoning))) AND ((ganglionic blockers OR hexamethonium) AND lung)

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	All Fields ▾	hexamethonium AND (toxicity OR adverse effects OR poisoning)	⊖	Show index list
AND ▾	All Fields ▾	(ganglionic blockers OR hexamethonium) AND lung	⊖	Show index list
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#3	Add	Search all [sb] Sort by: PublicationDate	27403291	23:58:38
#2	Add	Search 11834748[uid]	1	23:09:18

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- ☐ [Regulation of Cigarette Smoke Induction of IL-8 in Macrophages by AMP-activated Protein Kinase Signaling.](#)

Ko HK, Lee HF, Lin AH, Liu MH, Liu CI, Lee TS, Kou YR.

J Cell Physiol. 2015 Aug;230(8):1781-93. doi: 10.1002/jcp.24881.

PMID: 25503516

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- ☐ [Role of TRPV1 and P2X receptors in the activation of lung vagal C-fiber afferents by inhaled cigarette smoke in rats.](#)

Weng WH, Hsu CC, Chiang LL, Lin YJ, Lin YS, Su CL.

Mol Med Rep. 2013 Apr;7(4):1300-4. doi: 10.3892/mmr.2013.1300. Epub 2013 Jan 30.

PMID: 23443231

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- ☐ [Silencing of periostin inhibits nicotine-mediated tumor cell growth and epithelial-mesenchymal transition in lung cancer cells.](#)

Wu SQ, Lv YE, Lin BH, Luo LM, Lv SL, Bi AH, Jia YS.

Mol Med Rep. 2013 Mar;7(3):875-80. doi: 10.3892/mmr.2013.1267. Epub 2013 Jan 9.

PMID: 23314871

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- ☐ [Airway irritation and cough evoked by inhaled cigarette smoke: role of neuronal nicotinic acetylcholine receptors.](#)

9.

Lee LY, Burki NK, Gerhardstein DC, Gu Q, Kou YR, Xu J.

Pulm Pharmacol Ther. 2007;20(4):355-64. Epub 2006 Oct 18.

PMID: 17137814

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- ☐ [Nicotine and angiogenesis: a new paradigm for tobacco-related diseases.](#)

10.

Cooke JP, Bitterman H.

Ann Med. 2004;36(1):33-40. Review.

PMID: 15000345

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11.

McLellan F.

Lancet. 2001 Aug 25;358(9282):646. No abstract available.

PMID: 11530164

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- ☐ [Human subjects. Volunteer's death prompts review.](#)

12.

Marshall E.

Science. 2001 Jun 22;292(5525):2226-7. No abstract available.

PMID: 11423623

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- ☐ [Parasympathetic component of 5-hydroxytryptamine-induced pulmonary dysfunctions in healthy calves.](#)

13.

Linden AS, Desmecht DJ, Amory H, Lekeux PM.

Am J Vet Res. 1996 Jun;57(6):896-901.

PMID: 8725820

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☐ [Drug-induced lung disease.](#)

24. Davies PD.

Br J Dis Chest. 1969 Apr;63(2):59-70. Review. No abstract available.

PMID: 4388934

[Similar articles](#)

☐ [Reactivity of the bronchial tree to different stimuli.](#)

25. de Vries K, Booy-Nord H, Lende R vd, van Lookeren Campagne JG, Orie NG.

Bronches. 1968 Nov-Dec;18(6):439-52. No abstract available.

PMID: 4394341

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☐ [Fibrous healing of old iatrogenic pulmonary edema \("hexamethonium lung"\).](#)

26. HEARD BE.

J Pathol Bacteriol. 1962 Jan;83:159-64. No abstract available.

PMID: 13905765

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☐ [Bronchospasm associated with the use of a combination of succinylcholine and mylaxen to produce muscular relaxation.](#)

27.

SELVIN B, HOWLAND WS.

Anesth Analg. 1959 Sep-Oct;38:332-4. No abstract available.

PMID: 14444777

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☐ [Hexamethonium lung: report of a case associated with pregnancy.](#)

28. COCKERSOLE FJ, PARK WW.

J Obstet Gynaecol Br Emp. 1956 Oct;63(5):728-34. No abstract available.

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[Br Heart J.](#) 1954 Jan;16(1):101-8.

Lung changes during hexamethonium therapy for hypertension.

[DONIACH I](#), [MORRISON B](#), [STEINER RE](#).PMID: 13126364 PMCID: [PMC503873](#)[Indexed for MEDLINE] [Free PMC Article](#)

MeSH terms, Substances

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Comprehensive searches usually require multiple information sources

- Different sources have areas of specialization but may overlap
- Many sources are available from NIH Library – some must be searched by NIH Library staff who may request a CAN number
- Examples of some information sources follow; see websites for tutorials & more information
 - different versions of these sources may be available with varying coverage and capabilities
 - many other sources may also be important for a given search

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Embase™ vs. PubMed

- “Lung Changes During Hexamethonium Therapy for Hypertension”, British Heart J, 1954

PubMed – doesn’t include abstract, *‘toxicity’* or *‘adverse effects’*

Embase – includes abstract, *‘dyspnea’* & *‘edema’* (& British spellings),
but not *‘toxicity’* or *‘adverse effects’*

- “Hexamethonium lung; report of a case associated with pregnancy”, J Obstet Gynaecol Br Emp, 1956

PubMed – no abstract, but good MeSH indexing terms

Hexamethonium Compounds/*adverse effects

Embase – includes ‘edema’ & abstract, but not ‘adverse effects’: “...a woman of 37, treated with hexamethonium compounds...died after the birth of a live infant...Treatment with hexamethonium drugs... from the 17th week. Severe, ultimately fatal, respiratory disease developed during the 35th week...”

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Search for... e.g. 'heart attack' AND stress

AND ▾

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e.g. american heart



AND ▾

Author name ▾

e.g. watson j



AND ▾

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Population

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e.g. insulin

Comparison

e.g. placebo

Outcome

e.g. risk

Study design (or miscellaneous)

e.g. randomized controlled trial



Find best term

diabetes



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- ☒ diabetes complications
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- ☒ diabetes mellitus
822,106 records found
- ☒ diabetes adult onset
Use preferred term 'non insulin dependent diabet...'
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Use preferred term 'non insulin dependent diabet...'
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PICO Search

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Population

Intervention

e.g. insulin

Comparison

e.g. placebo

Outcome

e.g. risk

Study design (or miscellaneous)

e.g. randomized controlled trial

PV wizard

Drug
nameAlternative
drug namesAdverse
drug
reactionsSpecial
situationsHuman
limit

Drug name

e.g. Paracetamol

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Subheadings

- | | |
|---|---|
| <input checked="" type="checkbox"/> Adverse drug reaction | <input type="checkbox"/> Drug combination |
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Lung changes during hexamethonium therapy for hypertension

[Doniach I.](#), [Morrison B.](#), [Steiner R.E.](#)

British Heart Journal 1954 16:1 (101-108)

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Abstract

In a series of 54 cases of severe hypertension treated with parenteral hexamethonium bromide, (C6), 3 cases developed dyspnoea and patchy shadowing in the lung fields. Two of these patients died and at autopsy it was found that the lung lesions consisted of organized fibrinous pulmonary oedema. The changes in fact were those of 'carnification'. The oedema was attributed to mild attacks of left ventricular failure modified by the effect of C6 in lowering the blood pressure; and the treatment by prolonging life allowed the process of carnification to develop. The change. were not regarded as being directly attributable to Cf, and were not considered to be a contraindication to the use of this drug.

Drug Terms

hexamethonium %; hexamethonium bromide %;

Disease Terms

dyspnea %; edema %; heart left ventricle failure %; hypertension %; lung edema %; lung injury %;

Other Terms

autopsy %; blood pressure %; lung %; lung development %; patient %; therapy %;

Session Results / Record 2 of 3 Full record ▾[Add All to Clipboard >](#)[Print](#)

Record 2

[Similar records](#) | [Add to Clipboard](#) | [Email Record](#)[Back to results](#)[Previous](#) [Next](#)**Hexamethonium lung. Report of a case associated with pregnancy**Wallace Park W., Cockersole F.J.

Journal of obstetrics and gynaecology of the British Empire 1956 63:5 (728-734)

**Abstract**

The case is reported of a woman of 37, treated with hexamethonium compounds for severe hypertension during her 8th pregnancy. She died after the birth of a live infant, in the 36th week. Treatment with hexamethonium drugs had been continuous, in increasing dosage, from the 17th week. Severe, ultimately fatal, respiratory disease developed during the 35th week. Necropsy showed nephrosclerosis, hypertrophy of the left ventricle, and a state of 'solid oedema' and widespread fine fibrosis throughout both lungs. Microscopically the condition was one of non-infected, fibrinous, pulmonary oedema with organization and areas of fibrosis. The possible mechanism of development of the lesion is discussed.

Drug Terms

BCG vaccine % hexamethonium %

Disease Terms

edema % fibrosis % hypertension % hypertrophy % lung edema % nephrosclerosis % respiratory tract disease %

Other Terms

autopsy % female % heart left ventricle % infant % lung % pregnancy % solid %

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- **“had lung toxicity as the first side effect of hexamethonium” (JHU Report, 7/01)**
- mine for comparative drug information, i.e. hypoglycemic data for anti-diabetes drugs as compared with Metformin

Lexicomp / AHFS - clinical decision support tools and databases including detailed drug monographs from AHFS (American Hospital Formulary System from ASHP, the American Society of Health-System Pharmacists)

- see <http://www.wolterskluwer CDI.com/lexicomp-online/>
- User Guide at <http://online.lexi.com/lco/help/lco-ug.pdf>

Up To Date - clinical decision support system for point-of-care; etiology, diagnosis & treatment questions; peer-reviewed text includes drug and evidenced-based information; currency varies; references have links to NIH full-text subscriptions

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Evidence-Based Information: Secondary Sources

Cochrane Library www.cochranelibrary.com - Regularly updated subscription-based collection for practitioners, patients & policy makers; includes:

- Systematic reviews of interventions; extensive abstracts in PubMed; search for: “Cochrane Database Syst Rev”[TA]
- Evaluations of effectiveness of health care interventions
- Clinical trial reports (published/unpublished)
- NIH staff have access via NIH Library
- Free in some countries

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- registry maintained by NIH; not limited to NIH-funded research

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- approx. 20 registries, maintained by World Health Organization,
<http://www.who.int/ictrp/en/>

Cochrane Library – published & unpublished clinical trial reports

Pharmaprojects (formerly Pipeline) – subscription based drugs-in-development database; detailed drug profiles including therapy, mechanism, biological targets, development history & clinical trial information

FAQ <http://nih-pipeline.citeline.com/CpHelp.aspx> ; Quick Start
<https://nih-pipeline.citeline.com/Documents/Quick%20Start.pdf>

Despite policies, many trials are not properly registered

Mann E, et al, *Compliance with trial registration in 5 core journals of clinical geriatrics*, Age Ageing 2014; PMID 24982096
<http://www.ncbi.nlm.nih.gov/pubmed/24982096>

Hakala A, et al, *Accessibility of trial reports for drugs stalling in development*, BMJ 2015; PMID 25752879
<http://www.ncbi.nlm.nih.gov/pubmed/25752879>

Weber WE, et al, *Trial Registration 10 years on*, BMJ 2015; PMID 26149708
<http://www.ncbi.nlm.nih.gov/pubmed/26149708>

Take-away: read critically; data & insights can come from both old and new resources

Prasad V, et al, *A decade of reversal: an analysis of 146 contradicted medical practices*, Mayo Clin Proc 2013; PMID 23871230
<http://www.ncbi.nlm.nih.gov/pubmed/23871230>

ClinicalTrials.gov is a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world.

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X

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e.g., NCT number, drug name, investigator name

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TOXNET - <http://toxnet.nlm.nih.gov> - cluster of databases covering toxicology, hazardous chemicals, environmental health & related areas from NLM – for more info see <http://www.nlm.nih.gov/pubs/factsheets/toxnetfs.html>

Texts & References – either in print or online:

- NCBI Bookshelf – free online books, available by clicking the arrow next to the PubMed search window to search ‘Books’-
<http://www.ncbi.nlm.nih.gov/books>
- Hexamethonium toxicity wasn’t mentioned in the last 4 editions of Goodman & Gillman, or in the current edition of Fishman’s Pulmonary Medicine – but was included in a previous edition of Fishman’s text (JHU Report, 7/01)

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2. Excitatory action of lead on rat sympathetic preganglionic neurons in vitro and in vivo. Lai CC; Lin HH; Chen CW; Chen SH; Chiu TH Life Sci. 2002, Jul 19; 71(9):1035-45. [Life sciences] [PubMed] PubMed Citation 	DART More Results (52)	 Select Record
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Washington (DC): National Academies Press (US); 2016 Sep 26.



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- Scopus covers much of the content of Compendex, but lacks the extensive subject-specific indexing

SciFinder – chemistry information subscription database from Chemical Abstracts; menu-based end-user access; STN staff can request access from NIH Library



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“Web Search: Thinking Beyond Google” NIH Library class – handout

<https://nihlibrary.nih.gov/resources/subject-guides/web-search-thinking-beyond-google>

“Google and Bing for Researchers”, Daniel Russell of Google and Duane Forrester of Bing/Microsoft, NIH lecture, 2/6/13,

<http://videocast.nih.gov/launch.asp?17791>

“How to solve impossible problems: Daniel Russell’s awesome Google search techniques”, John Tedesco, 6-21-12,

<http://www.johntedesco.net/blog/2012/06/21/how-to-solve-impossible-problems-daniel-russells-awesome-google-search-techniques>

Become a Google Power Searcher – free online courses from Google, may require free gmail account, <http://www.powersearchingwithgoogle.com/>

John Tedesco

Investigative Reporter for the San Antonio Express-News

How to solve impossible problems: Daniel Russell's awesome Google search techniques

Daniel Russell stood in front of a crowd of [investigative journalists in Boston](#) last week and showed us this picture of a random skyscraper in an unknown city:



Russell posed a riddle:

What's the phone number of the office where this picture was snapped?

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Connect:

Bing www.bing.com ; > **Preferences** <http://www.bing.com/account> or > hamburger button at upper right > 'Settings' > 'Results' > change from 'Auto' to 50 > 'Save';

Help <http://onlinehelp.microsoft.com/en-US/bing/ff808535.aspx>

Advanced <http://help.bing.microsoft.com/#apex/18/en-US/10001/-1>
<http://help.bing.microsoft.com/#apex/18/en-US/10002/-1>

Exalead www.exalead.com/search/ - allows **true proximity searching**, **truncation**, & **phonetic searching**; Information > Click 'Help' at bottom left for FAQ

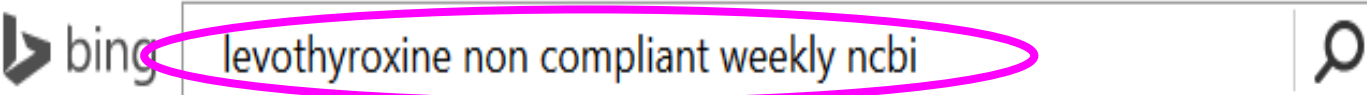
Advanced > 'advanced search' > menu of options;

Preferences (upper right) or www.exalead.com/account/preferences/ > change 'Results per page' from '10' to '100' > 'Save my preferences';

DuckDuckGo <https://duckduckgo.com> - preserves privacy; doesn't track users questions or personalize search results; other privacy-oriented search engines are:

Startpage www.startpage.com – Google results with privacy protection

Ixquick www.ixquick.eu – meta-search engine results with privacy protection



Also try: [Non-Compliant Diabetic Patient](#) · [Non-Compliant Behavior](#) · [Non-Compliance](#)

46,500 RESULTS

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★ [Once **weekly** thyroxine treatment as a strategy to treat non ...](#)

[www.ncbi.nlm.nih.gov](#) › [NCBI](#) › Literature

... the diagnosis of **non-compliance**. Supervised once **weekly** oral ... of **levothyroxine**--Case ... National Center for Biotechnology Information ...

[SYNTHROID \(LEVOTHYROXINE SODIUM\) TABLET \[ABBVIE INC.\]](#)

[dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=1E11AD30-1041-4520...](#) ▼

... poor **compliance**, ... **Non** Steroidal Anti-Inflammatory ... with gradual dose increments at 4-6 **week** intervals. The **levothyroxine** sodium dose is generally adjusted ...

★ [Nonadherence to Medication in Hypothyroidism: A Case Report](#)

[www.ncbi.nlm.nih.gov](#) › [NCBI](#) › Literature

The case reports suggest that a **weekly** total dose of **levothyroxine** ... Once **weekly** thyroxine treatment as a strategy to treat **non-compliance**. ... Simple NCBI Directory.

[Management Strategies for Hypothyroidism in Noncompliant ...](#)

[academic.research.microsoft.com/Paper/10917098.aspx](#) ▼

... of 125 micrograms/day. The patient was very **non-compliant** with her daily oral ... given the **weekly** dose of **levothyroxine** 700 micrograms ...

Related searches

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by S Rangan - 2007 - Cited by 17 - Related articles

Once **weekly** thyroxine treatment as a strategy to treat **non-compliance** Mandel S J, Brent G A, Larsen P R. **Levothyroxine** therapy in patients with thyroid ...[Nonadherence to Medication in Hypothyroidism: A Case Report](#)[www.ncbi.nlm.nih.gov > ... > v.12\(3\); 2010](#) ▾ National Center for Biotechnology Information

by RC Kandukuri - 2010 - Related articles

We are sorry, but NCBI web applications do not support your browser, and may not work properly. Please use a supported browser to access the site. Mr A was started on intravenous **levothyroxine**, quetiapine, and citalopram. Once **weekly** thyroxine treatment as a strategy to treat **non-compliance**.[\[Hypothyroidism due to pseudo-malabsorption of **levothyroxine** ...](#)[www.ncbi.nlm.nih.gov/pubmed/19941234](#) ▾ National Center for Biotechnology Information

by K Müssig - 2009

Nov 25, 2009 - In some patients, hypothyroidism is refractory to oral **levothyroxine** ... In **non-compliant** patients, supervised once **weekly levothyroxine** ...[Treating primary hypothyroidism with **weekly** doses of **levothyroxine** ...](#)[www.ncbi.nlm.nih.gov/pubmed/22790470](#) ▾ National Center for Biotechnology Information

by A Bornschein - 2012 - Cited by 2 - Related articles

OBJECTIVE: **Compliance** to **levothyroxine** treatment in hypothyroidism is compromised by **daily** ... Fourteen females were assigned to **daily** or **weekly** doses of LT4. ... TSH remained unchanged and there were **no** hyperthyroidism symptoms or ...[Case report: increased **levothyroxine** requirement in a patient with ...](#)[www.ncbi.nlm.nih.gov/pubmed/15251601](#) ▾ National Center for Biotechnology Information

NCBI resource list - > '*Resources*' above PubMed search window >

'All Resources' > list <https://www.ncbi.nlm.nih.gov/guide/all/>

Search NCBI databases > click down arrow next to 'PubMed'

> Search 'All Databases'

NCBI YouTube channel - tutorials <http://www.youtube.com/ncbinlm>

NIH Library Bioinformatics - from NIH Library home page:

> 'Services' > 'Bioinformatics Support'

<https://nihlibrary.nih.gov/services/bioinformatics-support>

> 'Services' > 'Bioinformatics Support' > 'Online Bioinformatics Tutorials'

<https://nihlibrary.nih.gov/services/bioinformatics-support/online-bioinformatics-tutorials>

> 'Services' > 'Bioinformatics Support' > 'Current Classes'

- information about the NIH Library's Bioinformatics classes

Keytruda - "FDA approves first cancer treatment for any solid tumor with a specific genetic feature", 5/23/17

<https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm560167.htm>

National Center for
Biotechnology Information

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Databases

[Assembly](#)

A database providing information on the structure of assembled genomes, assembly names and other meta-data, statistical reports, and links to genomic sequence data.

[BioCollections](#)

A curated set of metadata for culture collections, museums, herbaria and other natural history collections. The records display collection codes, information about the collections' home institutions, and links to relevant data at NCBI.

[BioProject \(formerly Genome Project\)](#)

A collection of genomics, functional genomics, and genetics studies and links to their resulting datasets. This resource describes project scope, material, and objectives and provides a mechanism to retrieve datasets that are often difficult to find due to inconsistent annotation, multiple independent submissions, and the varied nature of diverse data types which are often stored in different databases.

[BioSample](#)

The BioSample database contains descriptions of biological source materials used in experimental assays.

[BioSystems](#)

Database that groups biomedical literature, small molecules, and sequence data in terms of biological relationships.

[Bookshelf](#)

A collection of biomedical books that can be searched directly or from linked data in other NCBI databases. The collection includes biomedical textbooks, other scientific titles, genetic resources such as *GeneReviews*, and NCBI help manuals.

[ClinVar](#)

A resource to provide a public, tracked record of reported relationships between human variation and observed health status with supporting evidence. Related information in the [NIH Genetic Testing Registry \(GTR\)](#), [MedGen](#), [Gene](#), [OMIM](#), [PubMed](#) and other sources is accessible through hyperlinks on the records.

[ClinicalTrials.gov](#)

A registry and results database of publicly- and privately-supported clinical studies of human participants conducted around the world.

[CloneDB \(formerly Clone Registry\)](#)

A database that integrates information about clones and libraries, including sequence data, map positions and distributor information.

[Computational Resources from NCBI's Structure Group](#)

A centralized page providing access and links to resources developed by the Structure Group of the NCBI Computational Biology Branch (CBB). These resources cover databases and tools to help in the study of macromolecular structures, conserved domains and protein

Bioinformatics Support

[Current Classes](#)

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[Reserve a High Performance Bioinformatics Workstation](#)

[Bioinformatics Resources Registration](#)

[Biosocial Networking](#)

[Bioinformatics Consult](#)

[Computational Molecular Biology Resources: Automated Discovery and Categorization](#)

[Computational Molecular Biology: Curated List through](#)

Bioinformatics Support Program



Dr. Medha Bhagwat, NIH Library Bioinformatics Support Program Coordinator, received the NIH Office of the Director Honor Award "in recognition of outstanding leadership in developing a nationally renowned library-based bioinformatics support program to facilitate NIH intramural scientific advances."

The NIH Library's Bioinformatics Support Program was developed to provide researchers with powerful tools to analyze and understand the biological significance of a variety of data. The program is conducted by an expert bioinformatics trainer, Dr. Medha Bhagwat.

Learn more about bioinformatics work at NIH in the August 2009 issue, page 10, of [The NIH Catalyst](#) and from the November 2010 issue, page 3, of [The NIH Catalyst](#)

Bioinformatics Support

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[Entrez Gene Tutorial](#)

[NCBI RefSeq group](#)

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[UCSC Genome Bioinformatics](#) [Ⓐ]

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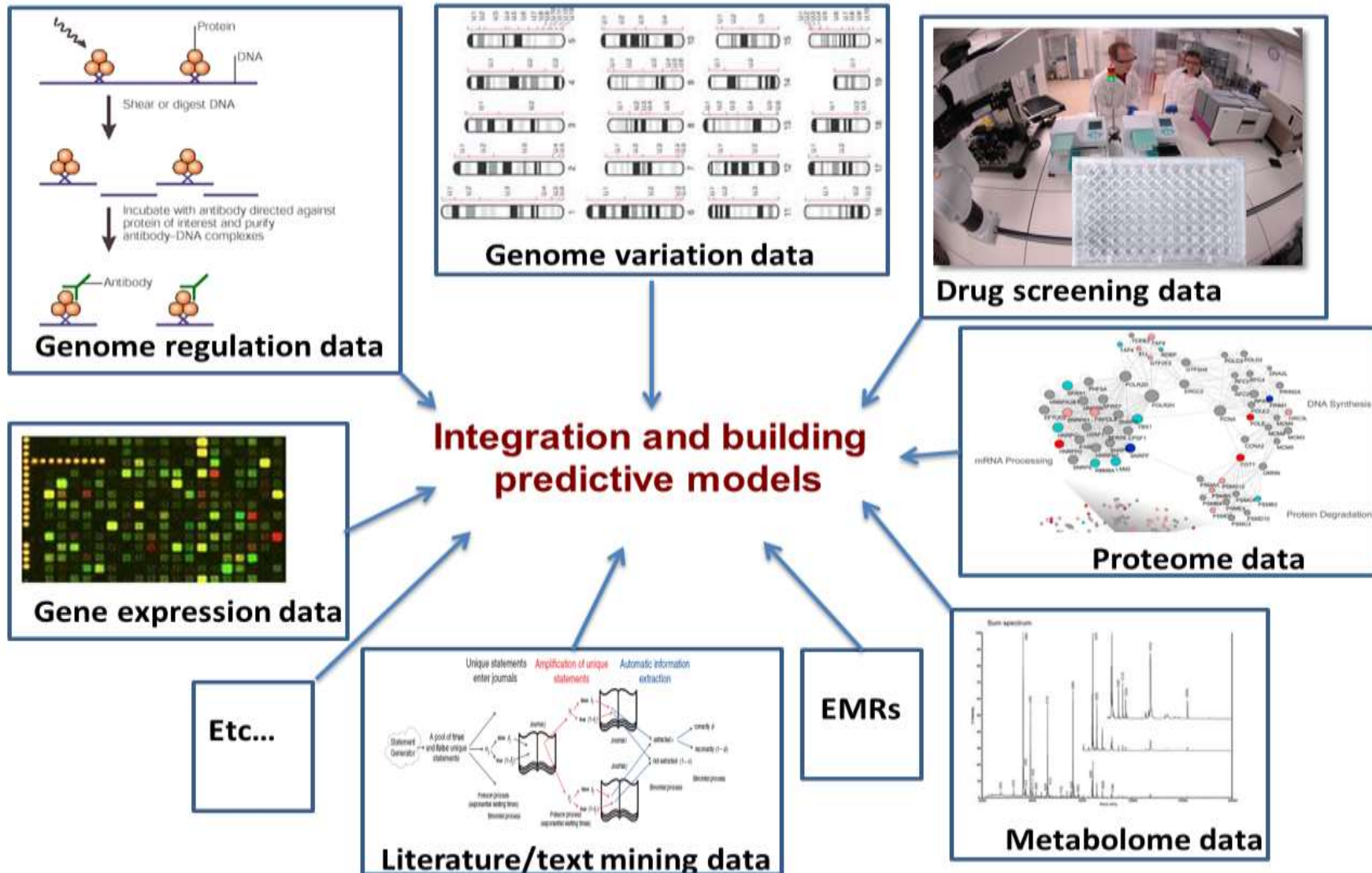
Networks of data and information mined for the discovery of disease mechanisms and new therapeutics - NIH lectures:

- The Emerging Network of Data for Understanding the Interactions of Genes and Drugs, Russ Altman, NIH, 10/12/11, <http://videocast.nih.gov/launch.asp?16900>
- Genomic Networks in Development and Cancer: Resolving Biomarkers and Therapeutic Targets from a Cloud of Data, Kevin White, NIH, 2/14/12, <http://videocast.nih.gov/launch.asp?17107>
- Translational Bioinformatics: Transforming 300 Billion Points of Data into Diagnostics, Therapeutics, and New Insights into Disease, Atul Butte, NIH, 6/20/12 <http://videocast.nih.gov/launch.asp?17321>

NIH Precision Medicine Initiative ‘All of Us’ – includes plans for a research cohort of > 1M volunteers who will share genetic data, biological samples and diet/lifestyle info

<http://www.nih.gov/precisionmedicine/>

Defining Networks, Mining Networks



from 'Genomic Networks in Development and Cancer', Kevin White, NIH Seminar, 2/14/12,
<http://videocast.nih.gov/launch.asp?17107>

Data Management – emerging subject in clinical research; NIH Library Data Services guide <http://nihlibrary.campusguides.com/dataservices/> includes:
Introduction to Data management; Finding and Re-using Scientific Research Data; Research Data Description and Organization; Preservation, Retention, and Storage of Digital Data; and data visualization topics; examples of content include:

Data Life Cycle: Proposal planning & writing; Project start up; Data collection; Data analysis (possibly re-purpose data); Data sharing; End of project; Deposit data in data archive; Re-use data for data discovery – an iterative process, not linear

Pre-Project Data Management Plan - consider using open formats vs proprietary formats; data collection - consider collecting meta-data including synonyms and controlled vocabulary terms; many journals have requirements about depositing data in repositories, such as GEO or GenBank

HA Piwowar, RS Day, DB Fridsma, Sharing Detailed Research Data Is Associated with Increased Citation Rate, *PLoS ONE*, 2007; 2(3): e308, PMID 17375194, doi:10.1371/journal.pone.0000308
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1817752/>

Bibliometrics – statistical analysis of written publications, books or articles; used to measure the impact of an author, or within a subject area or a portfolio; NIH Library Bibliometric Services described at <http://nihlibrary.campusguides.com/bibliometrics>

Impact factor of a journal – ratio between citations to articles in that journal and number of articles published in a particular year – searchable from *Journal Citation Reports* from Web of Science (ISI)

h-index - attempts to measure an author's productivity and impact, based on the author's most cited papers and the number of citations received; an author with an h-index of 20 has written at least 20 papers which have each been cited at least 20 times

- available from Scopus and Web of Science (both subscription-based), and
- Publish or Perish website <http://www.harzing.com/pop.htm> - free; uses Google Scholar and Microsoft Academic Search

More information <http://nihlibrary.campusguides.com/c.php?g=38330&p=244518>

Google Scholar Metrics <http://scholar.google.com/intl/en-US/scholar/metrics.html>

MyRI – “Measuring *your* Research Impact” - Open Access toolkit for bibliographic training and awareness <http://myri.conul.ie/>

Scholarometer <http://scholarometer.indiana.edu/> - social tool to facilitate citation analysis

Systematic review - review of a clearly formulated question that uses systematic and explicit methods

- to identify, select, and critically appraise relevant research, and
- to collect and analyze data from the included studies;
- statistical methods or meta-analysis may or may not be used

NIH Library information for Systematic Reviews – includes gold standards, organizations, literature sources, scoring guides, documenting your work, protocols and protocol registries, and resources

<http://nihlibrary.campusguides.com/systematicreviews>

PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses)

- 27 item checklist, information flow diagram and Statement, links at

<http://www.prisma-statement.org/>

Finding What Works in Health Care: Standards for Systematic Reviews, Institute of Medicine, National Academies Press, 2011

<http://www.ncbi.nlm.nih.gov/books/NBK209518/>

Selected Clinical Information Resources

Name	Free?	Subject	Notes
PubMed	Y	biomedicine	a standard of biomedical search; MeSH; My NCBI
Embase	\$	biomedicine	larger than PubMed; international; conferences; Emtree
Web of Science	\$	Science	cited reference searching; conferences
Scopus	\$	Science	cited reference searching; conferences
Micromedex	\$	drugs/toxicology	drug monographs; PosIndex - poison control centers
Lexicomp/AHFS	\$	drugs/toxicology	detailed AHSP drug monographs
UpToDate	\$	clinical medicine	point-of-care decision support system
Cochrane	Y / \$	biomedicine	evidence-based medicine; clinical trials; reviews in PubMed
Guidelines.gov	Y	clinical medicine	evidence-based medicine
clinicaltrials.gov	Y	clinical trials	registered clinical trials
ICTRP	Y	clinical trials	registered clinical trials
Pharmaprojects	\$	drug development	mine drug profiles for clinical trial information
ToxNet	Y	toxicology	databases of toxicological information
NCBI Bookshelf	Y	biomedicine	full text
MedWatch	Y	drugs	FDA safety alerts
RePORTER	Y	research grants	NIH-supported research
PsychINFO	\$	psychology	psychological, social, behavioral information
Compendex	\$	engineering	devices & instrumentation information
Inspec	\$	engineering	devices & instrumentation information
PubMed Central	Y	biomedicine	full text
MedlinePlus	Y	medicine	consumer health information
Google Scholar	Y	science	full text articles & conference information
NCBI	Y	bioinformatics	sequences, genomics, etc.

Search Strategy - one general model

- 1) Break query into essential concepts
- 2) Find synonyms/alternate terms for the concepts – use controlled vocabularies if available
- 3) Expand, then reduce retrieval – group together synonyms for each concept with ‘OR’ logic; then ‘AND’ the concept groups together
- 4) Use as many information resources as necessary
- 5) Search for information to find more information:
 - Find key citations, possibly with Wikipedia (check the footnotes), Google, Bing, etc.;
 - Search for these key citations in PubMed/ Embase/ etc. to find controlled vocabulary terms to expand your synonym lists
 - Use these key citations in cited reference searching (Scopus/ Web of Science/ Google Scholar)
- 6) Repeat as necessary
- 7) Keep track of all searches and retrievals
- 8) Remove duplicate retrievals

Search Strategy Tips

Ask the Right Questions, the right way – the **PICO** outline can help organize search concepts & terms: Patient/Population and/or Problem; Intervention; Comparison/Control; Outcome or Effects

- The Literature Searching Process Protocol for Researchers, Thames Valley Health Libraries Network, Mar. 2006,

http://www.ieph.org/hase/Downloads/Lit_Search_Protocol_Researchers.pdf

Remove Duplicates - use bibliographic/reference management utilities including EndNote (NIH-wide subscription); NIH Library Endnote classes <https://nihlibrary.nih.gov/training/endnote> and <http://endnote.com/training>

- Reference management software compared; includes free options

http://en.wikipedia.org/wiki/Comparison_of_reference_management_software

Research Updates – set your searches to repeat automatically when the database is updated using MyNCBI in PubMed; check other databases for similar capabilities

- **You've identified and searched all relevant resources, and you understand their scope and coverage**
- **You understand how each search engine works, what it searches, and what assumptions it makes**
 - plurals and/or alternate spellings automatically included?
 - search terms automatically "OR"ed with each other?
 - Google & web search engine results may be inconsistent – many assumptions & relevancy rankings aren't disclosed
- **Your results include known relevant articles**
- **Different searchers/searches yield no new relevant results**

- Can you trust your search results?
- When is a search complete?
- These are difficult questions, best answered by
 - experience
 - following the guidelines & suggestions mentioned above
 - verifying your strategy & results
 - **collaborating with a reference librarian, and, if applicable, a pharmacist as well**

- ★ ***Guidelines for Determining an Adequate and Comprehensive Literature Search of Drug and Device Safety for Use by Investigator and Institutional Review Boards***, Institutional Review Board, Mount Sinai School of Medicine, 1/03,

http://www.mssm.edu/static_files/Old%20Sites/www.mssm.edu/cmca/pdf/SearchGuidelines.pdf

- includes overview, search log, summary & bibliography forms, lists of sources, & search technique suggestions

- ★ ***Literature Searching Guidelines Checklist for Researchers***, J Glover & M Gentry, Yale

http://library.medicine.yale.edu/sites/default/files/services/crs/Literature_Searching_Guidelines1.pdf

- very good checklist, includes many of the points discussed here

Final Notes & Acknowledgements

NIH Library email news - subscribe at

<https://list.nih.gov/cgi-bin/wa.exe?SUBED1=NIHLIB-L&A=1>

Acknowledgments: NIH Library staff Mary Ryan (ret.), Pam Sieving (ret.), Brian Brown, Chris Belter, Lisa Federer, Mehta Bhagwat, & Rex Robison; and the NIH Office of the Director, Office of Research Services

Please fill out the lecture evaluation at

<https://www.surveymonkey.com/r/jduberman> – **Thank You!!**

Questions or comments: jduberman@nih.gov